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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/445,803	12/13/1999	MARIO T. PHILIPP	TUL2AUSA	1398

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EXAMINER	
SWARTZ, RODNEY P	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 03/07/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/445,803	PHILIPP, MARIO T.	
	Examiner	Art Unit	
	Rodney P. Swartz, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31July2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-13,16,17,19,21,22,31-33,35,38,39,47-49,51-53 and 66-103* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-13,35,39,67,73-81,83,91-96,100 and 102* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *See Continuation Sheet* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's Response to Restriction, received 31July2001, paper#6, is acknowledged. Applicant elects, without traverse, Invention I, claims 10-13, 35, 39, 67, 73-81, 83, 91-96, 100, and 102, drawn to protein.

2. Currently, claims 10-13, 16, 17, 19, 21, 22, 31-33, 35, 38, 39, 47-49, 51-53, and 66-103 are pending. Claims 16, 17, 19, 21, 22, 31-33, 38, 47-49, 51-53, 66, 68-72, 82, 84-90, 97-99, 101, and 103 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

3. Claims 10-13, 35, 39, 67, 73-81, 83, 91-96, 100, and 102 are under consideration.

Drawings

4. This application has been filed with drawings which have been reviewed and approved by the Draftsperson.

Specification

5. The disclosure is objected to because of the following:

a) page 10, lines 13-14, ATCC Acc. Nos. are blank; in addition, Applicant's referral to the deposits of transformed *E. coli* is an insufficient assurance that all required deposits have been made and all the conditions of 37 CFR §§1.801-1.809 have been met. If the deposit has been made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and

registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest treaty, that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each nation. Amendment of the specification to recite the date of deposit and the complete name and full street address of the depository is required. Applicant's attention is directed to In re Lundeck, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR §§1.801-1.809 for further information concerning deposit practice.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 10-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are drawn to a method of recombinantly expressing "the P39.5 protein" or a fragment thereof. However, it is unclear what are the metes and bounds of the term "the P39.5 protein" because there is no designation of the source of the protein, i.e., bacteria, yeast, genus, species, strain, etc.

9. Claim 10-13 are rejected under 35 U.S.C. 112, second paragraph, lack of antecedent basis.

Claim 10 recites the limitation "the" P39.5 protein in line 1. There is insufficient antecedent basis for this limitation in the claim because there has been no prior recitation of "a" or any P39.5 protein to which "the" refers. It is recommended that the claim recite "a" P39.5 protein to obviate the rejection.

10. Claims 35, 73-79, and 91-95 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for induction of antibodies using P39.5 protein, and P7-1 protein, does not reasonably provide enablement for any/all other antigens expressed by any/all spirochetes as vaccines against Lyme Disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The nature of the invention - The claim is directed to a vaccine useful in the prophylaxis of Lyme Disease comprising a surface antigen expressed by the spirochete when it resides in the vertebrate host.

The state of the prior art - Prior art indicates successful vaccines against Lyme Disease microorganisms in animal models following extensive *in vivo* experimental testing. The prior art also teaches many embodiments which are not successful as vaccines *in vivo* even though *in vitro* studies indicate effects on the function/viability of spirochetes.

The amount of direction or guidance present - The instant specification teaches the purification and production of an antigenic protein (P39.5 and a fragment thereof, P7-1) which induces antibody formation in mice and monkeys and which binds to antibodies in animals and humans previously infected with Lyme Disease spirochetes. While the specification teaches *in vitro* killing assays using the antibodies to P39.5 and P7-1 proteins, the specification does not provide any examples of the claimed invention, i.e., *in vivo* vaccine. In fact, the only reference to

any *in vivo* data teaches away from an effective vaccine, "In contrast, no spirochetes of the JD1 strain could be killed either *in vitro* (by ADCK) or *in vivo*, in a tick-challenge experiment with mice immunized with rP7-1 and Ribi adjuvant" (page 47, lines 9-11).

The quantity of experimentation necessary - Therefore, the instant claims constitute merely an invitation to experiment without a reasonable expectation of success.

11. Claims 80 and 96 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for induction of antibodies using P39.5 protein, and P7-1 protein, does not reasonably provide enablement for a method of vaccinating a human or animal against Lyme Disease comprising administration of an effective amount of a P39.5 protein, P1-1, P3-1, P6-1, P7-1, P9-1, P12-1, fusion protein, or fragment thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The nature of the invention - The claims are directed to a method of vaccinating a human or animal against Lyme Disease comprising administering a composition comprising an effective amount of P39.5, P1-1, P3-1, P6-1, P7-1, P9-1, P12-1, fusion protein, or fragment thereof.

The state of the prior art - The prior art indicates successful methods of vaccination against Lyme Disease microorganisms in animal models following extensive *in vivo* experimental testing. The prior art also teaches many embodiments which are not successful as methods of vaccinating *in vivo* even though *in vitro* studies indicate effects on the function/viability of spirochetes.

The amount of direction or guidance present -The instant specification teaches the purification and production of an antigenic protein (P39.5 and a fragment thereof, P7-1) which induces antibody formation in mice and monkeys and which binds to antibodies in animals and humans previously infected with Lyme Disease spirochetes. While the specification teaches *in vitro* killing assays using the antibodies to P39.5 and P7-1 proteins, the specification does not provide any examples of the claimed invention, i.e., *in vivo* vaccine. In fact, the only reference to any *in vivo* data teaches away from an effective vaccine, "In contrast, no spirochetes of the JD1 strain could be killed either *in vitro* (by ADCK) or *in vivo*, in a tick-challenge experiment with mice immunized with rP7-1 and Ribi adjuvant" (page 47, lines 9-11).

The presence or absence of working examples - Thus, the instant claim constitute merely an invitation to experiment without a reasonable expectation of success.

12. Claims 81 and 100 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for detection of Lyme Disease in humans using P39.5 and rP7-1, does not reasonably provide enablement for detection using other fragments, homologs, analogs, or fusion proteins of P39.5 or P7-1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The nature of the invention - a kit for diagnosing infection with *B. burgdorferi* in a human or animal comprising a P39.5 protein or fragment thereof.

The state of the prior art - The prior art teaches antigens utilized for diagnosing infection by *B. burgdorferi*. However, the art also teaches that not all antigens are used successfully diagnose *B. burgdorferi* infection.

The amount of direction or guidance present - The instant specification teaches detection of antibodies in the serum of humans with Lyme Disease using whole P39.5 protein or the

specific fragment P7-1. However, the specification does not teach the identity of the epitopes responsible for this ability, nor where on the P39.5 whole molecule such capability resides, other than that the specific fragment P7-1 has the capability. Thus, without knowing identifying the required epitopes necessary for detection of infection by *B. burgdorferi*, the claim invention constitutes merely an invitation to experiment in order to determine what fragments, analogs, homologs, and fusion proteins other than P39.5 and P7-1 can be utilized for detection of infection.

13. Claims 67 and 73-83 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are drawn to analogs, homologs, and fusion proteins which have ≥80% homology with SEQ ID NO; 2 or 14. However, it is unclear what are the metes and bounds of determining the type of homology being claimed, i.e., consecutive amino acids, every second or third residue, etc, and it unclear what is the function of such constructs.

One of the embodiments (d) of claim 67 is drawn to a fragment of a protein comprising either SEQ ID NO:2 (embodiment b) or 14 (embodiment c). Because of the open language "comprising", the claimed protein embodiment (d) may be a fragment of the nondefined regions of embodiment b or c. Thus, embodiment d is indefinite for both structure and function.

Embodiments j and k of claim 67 are likewise indefinite for both structure and function for the same reasoning as pertains to embodiment d.

It is unclear how the protein of embodiment k can be both a recombinant protein and a chemically synthesized protein at the same time.

14. Claim 102 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: how does one determine the amount of test compound bound to said protein or fragment?

15. Claim 39 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim is drawn to a protein or fragment thereof of "a *Borrelia*" cassette string, selected from the group consisting of P1-1, P3-1, P6-1, P7-1, P9-1, and P12-1.

The specification only teaches and provides an example of such a cassette string from one species of *Borrelia*, *i.e., B. garinii* IP90. However, the claim language, "a" *Borrelia*, encompasses all of the *Borrelia* genus. Thus, this one example in the specification does not reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of all cassette strings from all species of *Borrelia*.

Claim Rejections - 35 USC § 102

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

17. Claims 10-13, 35, 39, 67, 73, 74-83, 91-94, 96, 100, and 102 are rejected under 35 U.S.C. 102(b) as being anticipated by Zhang et al (*Cell*, 89:275-285, April, 1997).

The claims are drawn to proteins comprising fragments of P39.5, SEQ ID NO:2 or SEQ ID NO:14, vaccines composition comprising said fragments, methods of immunizing animals with said compositions, methods of identify compounds which bind to said fragments.

Zhang et al teach the claimed inventions by teaching proteins comprising fragments of SEQ ID NO:2 and SEQ ID NO:14 (Figure 2C), recombinant production of said proteins, immunizing of animals with said proteins, detection of antibodies which bind to said proteins, and fusion proteins of said proteins (**Experimental Procedures,** pages 283-284).

Conclusion

18. No claims are allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rodney P. Swartz, Ph.D., whose telephone number is (703) 308-4244. The examiner can normally be reached on Monday through Thursday from 5:30 AM to 4:00 PM EST.

If attempts to reach the Examiner by telephone are unsuccessful, the examiner's supervisor, Lynette F. Smith, can be reached on (703)308-3909. The facsimile telephone number for the Art Unit Group is (703)308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the group receptionist whose telephone number is (703)308-0196.

RODNEY P SWARTZ, PH.D
PRIMARY EXAMINER
Art Unit 1645

March 6, 2002